

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously amended) A method of preparing bimodal meso/macroporous siliceous materials comprising combining an organic polyol silane precursor with one or more additives under conditions suitable for hydrolysis and condensation of the precursor to a siliceous material and for phase separation to occur before gelation, wherein the one or more additives are one or more water-soluble polymers and wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to 10.
2. (Original) The method according to claim 1, wherein the one or more additives are water soluble polymers selected from one or more of polyethers, polyalcohols, polysaccharides, poly(vinyl pyridine), polyacids, polyacrylamides and polyallylamine.
3. (Original) The method according to claim 2, wherein the one or more additives are water soluble polymers selected from one or more of polyethylene oxide (PEO), polyethylene glycol (PEG), amino-terminated polyethylene oxide (PEO-NH₂), amino-terminated polyethylene glycol (PEG-NH₂), polypropylene glycol (PPG), polypropylene oxide (PPO), polypropylene glycol bis(2-amino-propyl ether) (PPG-NH₂), polyvinyl alcohol, poly(acrylic acid), poly(vinyl pyridine), poly(N-isopropylacrylamide) (polyNIPAM) and polyallylamine (PAM).
4. (Original) The method according to claim 3, wherein the one or more additives are water soluble polymers selected from one or more of PEO, PEO-NH₂, PEG, PPG-NH₂, polyNIPAM and PAM.

5. (Original) The method according to claim 3, wherein the one or more additives are water soluble polymers selected from one or more of PEO, PEO-NH₂ and polyNIPAM.
6. (Original) The method according to claim 1, wherein the one or more additives is a mixture of water soluble polymers,
7. (Original) The method according to claim 6 wherein the mixture of water soluble polymers comprises PEO and PEO-NH₂.
8. (Original) The method according to claim 5, wherein the one or more additives is PEO.
9. (Original) The method according to claim 8, wherein the PEO has a molecular weight that is greater than about 10,000 g/mol.
10. (Original) The method according to claim 9, wherein the PEO is used at a concentration of greater than about 0.005 g/mL of final solution.
11. (Original) The method according to claim 5, wherein the one or more additives is PEO-NH₂.
12. (Original) The method according to claim 11, wherein the PEO-NH₂ has a molecular weight that is greater than about 3,000 g/mol and is used at a concentration of about 0.005 g/mL of final solution.
13. (Original) The method according to claim 5, wherein the one or more additives is poly(N-isopropylacrylamide).

14. (Original) The method according to claim 13, wherein the poly(N-isopropylacrylamide) has a molecular weight that is about 10,000 g/mol and is used at a concentration of about 0.005 g/mL of final solution.

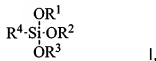
15. – 36. (Previously Cancelled)

37. (Original) The method according to claim 1, wherein the organic polyol silane precursor is selected from the group consisting of diglycerylsilane (DGS), monosorbitylsilane (MSS), monomaltosylsilane (MMS), dimaltosylsilane (DMS) and dextran-based silane (DS).

38. (Previously amended) The method according to claim 1, wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives in aqueous solutions and with optional sonication to assist in dissolution.

39. (Previously amended) A method of preparing siliceous materials with low shrinkage characteristics comprising:

(a) combining an aqueous solution of one or more compounds of Formula I:



wherein OR^1 , OR^2 and OR^3 are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide Si-OH groups; and R^4 is group that is not hydrolyzed under normal sol-gel conditions, with an aqueous solution of an organic polyol silane precursor;

(b) adjusting the pH of the solution in (a) to about 4-11.5;

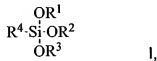
(c) allowing the solution of (b) to gel;

(d) aging the gel of (c); and

(e) drying the aged gel in air.

40. (Original) A siliceous material prepared using the method according to claim 1.

41. (Previously amended) A method of preparing monolithic bimodal meso/macroporous silica materials comprising combining an organic polyol silane precursor with one or more additives selected from one or more water-soluble polymers and one or more compounds of Formula I:

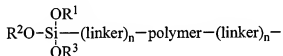


wherein OR¹, OR² and OR³ are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide Si-OH groups, R⁴ is group

$\begin{array}{c} \text{OR}^1 \\ | \\ \text{R}^2\text{O-Si-(linker)}_n\text{-polymer-(linker)}_n\text{-} \\ | \\ \text{OR}^3 \end{array}$

selected from polymer-(linker)_n- and and n = 0-1, under conditions suitable for hydrolysis and condensation of the precursor to a siliceous material and for phase transition to occur before gelation, wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to 10.

42. (Original) The method according to claim 41, wherein R⁴ is



43. (Original) The method according to claim 42, wherein the linker group is a C₁₋₄alkylene group and n is 1.

44. (Original) The method according to claim 42, wherein OR¹, OR² and OR³ are the same and are selected from C₁₋₄alkoxy.

45. (Original) The method according to claim 42, wherein the polymer is PEO.

46. (Original) The method according to claim 41 wherein the compound of Formula I is selected from the group consisting of:

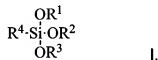
$(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)_2]_2$, $p \sim 4-5$, average MW 200 (Compound **5a**);
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)_2]_2$, $p \sim 13$, average MW 600 (Compound **5b**);
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)_2]_2$, $p \sim 44$, average MW 2000 (Compound **5c**); and
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)_2]_2$, $p \sim 227$, average MW 10,000 (Compound **5d**).

47. (Original) The method according to claim 41, wherein the water soluble polymer is selected from one or more of PEO, PEO-NH₂ and poly(NIPAM).

48. (Original) A meso/macroporous silica monolith prepared using the method according to claim 41.

49.-53. (Previously cancelled)

54. (Previously amended) A method of preparing a bimodal meso/macroporous monolithic silica chromatographic column comprising placing a solution comprising an organic polyol silane precursor and one or more additives selected from one or more water-soluble polymers and one or more compounds of Formula I:

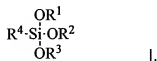


wherein OR¹, OR² and OR³ are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide a Si-OH group; R⁴ is group

selected from polymer-(linker)_n- and $\begin{array}{c} \text{OR}^1 \\ | \\ \text{R}^2\text{O-Si-}(\text{linker})_n\text{-polymer-}(\text{linker})_n\text{-} \\ | \\ \text{OR}^3 \end{array}$ and $n = 0-1$, in a column under conditions suitable for hydrolysis and condensation of the precursor to a siliceous material and for a phase transition to occur before gelation, wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to 10.

55. (Previously amended) The method according to claim 54, wherein the solution further comprises one or more substances, which provide cationic sites that counterbalance an anionic charge of the silica to reduce non-selective interactions

56. (Previously amended) A chromatographic column comprising a bimodal meso/macroporous silica monolith prepared by combining an organic polyol silane precursor and one or more additives selected from one or more water-soluble polymers and one or more compounds of Formula I:

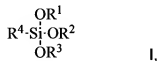


wherein OR¹, OR² and OR³ are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide Si-OH groups; R⁴ is group

$\begin{array}{c} \text{OR}^1 \\ | \\ \text{R}^2\text{O-Si-(linker)}_n\text{-polymer-(linker)}_n\text{-} \\ | \\ \text{OR}^3 \end{array}$ selected from polymer-(linker)_n- and and n = 0-1, under conditions suitable for hydrolysis and condensation of the precursor to a siliceous material and for phase transition to occur before gelation, wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to 10.

57. (Previously amended) A method of preparing a bimodal meso/macroporous silica column having an active biomolecule entrapped therein comprising combining:

- a polyol-silane derived silica precursor;
- one or more additives selected from one or more water soluble polymers and one or more compounds of Formula I:



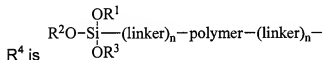
wherein OR¹, OR² and OR³ are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide Si-OH groups, R⁴ is group

selected from polymer-(linker)_n- and
$$\begin{array}{c} \text{OR}^1 \\ \text{R}^2\text{O}-\text{Si}-\text{(linker)}_n-\text{polymer}-(\text{linker})_n- \\ \text{OR}^3 \end{array}$$
 and n is 0-1; and

c) a biomolecule;

under conditions suitable for hydrolysis and condensation of the precursor to a siliceous material and for phase separation to occur before gelation, wherein the conditions comprise combining the organic polyol silane precursor with the one or more additives at a pH in the range of about 4 to 10.

58. (Original) The method according to claim 57, wherein the one or more additives is one or more water soluble polymers or one or more compounds of Formula I, wherein



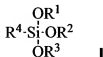
59. (Previously amended) The method according to claim 57, wherein the organic polyol silane silica precursor, one or more additives and biomolecules are also combined with a substance which provides cationic sites that counterbalance an anionic charge of the silica to reduce non-selective interactions.

60. (Original) A chromatographic column prepared using a method according to claim 57.

61. (Original) A method of performing immunoaffinity chromatography, sample cleanup, solid phase extraction or preconcentration of analytes, removal of unwanted contaminants, solid phase catalysis or frontal affinity chromatography comprising:

- (a) applying a sample to a column according to claim 60: and
- (b) performing immunoaffinity chromatography, sample cleanup, solid phase extraction or preconcentration of analytes, removal of unwanted contaminants, solid phase catalysis or frontal affinity chromatography.

62. (Previously amended) A method of preparing siliceous materials with enhanced protein stabilizing ability comprising combining an organic polyol silane precursor with one or more additives under conditions suitable for hydrolysis and condensation of precursor to a siliceous material, wherein the one or more additives is selected from one or more trifunctional silanes of Formula I:



wherein wherein OR^1 , OR^2 and OR^3 are the same or different and represent a group that is hydrolyzed under normal sol-gel conditions to provide a Si-OH group and R^4 is polyol-(linker)-.

63. (Previously amended) The method according to claim 62, wherein the polyol in R^4 is derived from sugar alcohols, sugar acids, saccharides, oligosaccharides or polysaccharides.

64. (Original) The method according to claim 63, wherein the polyol in R^4 is derived from allose, altrose, glucose, mannose, gulose, idose, galactose, talose, ribose, arabinose, xylose, lyxose, threose, erythrose, glyceraldehydes, sorbose, fructose, dextrose, levulose, sorbitol, sucrose, maltose, cellobiose, lactose, dextran (500-50,000 MW), amylose, pectin, glycerol, propylene glycol or trimethylene glycol.

65. (Previously amended) The method according to claim 64, wherein the polyol in R^4 is derived from glycerol, sorbitol, maltose, trehalose, glucose, sucrose, amylose, pectin, lactose, fructose, dextrose or dextran.

66. (Original) The method according to claim 65, wherein the polyol in R^4 is derived from glycerol, sorbitol, glucose, maltose or dextran.

67. (Original) The method according to claim 66, wherein the polyol in R⁴ is derived from glucose or maltose.
68. (Previously amended) The method according to claim 62 wherein the one or more additives is GluconamideSi (Compound 1) and/or MaltonamideSi (Compound 2).
69. (Original) The method according to claim 62, wherein the protein is a kinase, luciferase, or urease or is Factor Xa.
70. (Original) The method according to claim 69, wherein the protein is Src protein tyrosine kinase.
71. (Original) The method according to claim 62, further comprising combining the organic polyol silane precursor and one or more additives with a substrate for the protein to be entrapped.
72. (Original) The method according to claim 71, wherein the protein is a kinase and the substrate is a source of phosphate.
73. (Original) The method according to claim 72, wherein the substrate is ATP.
74. (Previously added) The method according to claim 59, wherein the substance which provides cationic sites that counterbalance an anionic charge of the silica to reduce non-selective interactions is aminopropyltriethoxysilane (APTES), PAM, PPG-NH₂ and/or PEG-NH₂.
75. (Previously added) The method according to claim 39, wherein OR¹, OR² and OR³ are the same or different and are derived from organic di- or polyols.

76. (Previously added) The method according to claim 75, wherein OR¹, OR² and OR³ are the same or different and are derived from sugar alcohols, sugar acids, saccharides, oligosaccharides or polysaccharides.

77. (Previously added) The method according to claim 75, wherein OR¹, OR² and OR³ are the same or different and are derived from allose, altrose, glucose, mannose, gulose, idose, galactose, talose, ribose, arabinose, xylose, lyxose, threose, erythrose, glyceraldehydes, sorbose, fructose, dextrose, levulose, sorbitol, sucrose, maltose, cellobiose, lactose, dextran (500-50,000 MW), amylose, pectin, glycerol, propylene glycol or trimethylene glycol.

78. (Previously added) The method according to claim 77, wherein OR¹, OR² and OR³ are the same or different and are derived from glycerol, sorbitol, maltose, trehalose, glucose, sucrose, amylose, pectin, lactose, fructose, dextrose and dextran.

79. (Previously added) The method according to claim 77, wherein OR¹, OR² and OR³ are the same or different and are derived from glycerol, sorbitol, maltose or dextran.

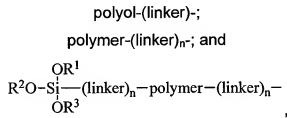
80. (Previously added) The method according to claim 39, wherein OR¹, OR² and OR³ are the same or different and are selected from C₁₋₄alkoxy, aryloxy and arylalkyleneoxy.

81. (Previously added) The method according to claim 80, wherein wherein OR¹, OR² and OR³ are the same or different and are selected from C₁₋₄alkoxy, phenoxy, naphthoxy and benzyloxy.

82. (Previously added) The method according to claim 81, wherein wherein OR¹, OR² and OR³ are the same or different and are selected from C₁₋₄alkoxy.

83. (Previously added) The method according to claim 82, wherein OR¹, OR² and OR³ are all ethoxy.

84. (Previously added) The method according to claim 39, wherein R⁴ is selected from the group consisting of:



wherein n is 0-1.

85. (Previously added) The method according to claim 84, wherein the polyol is an organic di- or polyol.

86. (Previously added) The method according to claim 85, wherein the polyol is selected from the group consisting of a sugar alcohol, sugar acid, saccharide, oligosaccharide and polysaccharide.

87. (Previously added) The method according to claim 86, wherein the polyol is a selected from the group consisting of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, ribose, arabinose, xylose, lyxose, threose, erythrose, glyceraldehydes, sorbose, fructose, dextrose, levulose, sorbitol, sucrose, maltose, cellobiose, lactose, dextran, (500-50,000 MW), amylose, pectin, glycerol, propylene glycol and trimethylene glycol.

88. (Previously added) The method according to claim 87, wherein the polyol is selected from the group consisting of glycerol, sorbitol, maltose, trehalose, glucose, sucrose, amylose, pectin, lactose, fructose, dextrose and dextran.

89. (Previously added) The method according to claim 88, wherein the polyol is selected from the group consisting of glycerol, sorbitol, glucose, maltose and dextrose.

90. (Previously added) The method according to claim 84 wherein the polymer is a water soluble polymer.

91. (Previously added) The method according to claim 90, wherein the polymer is selected from the group consisting of polyethylene oxide (PEO), polyethylene glycol (PEG), amino-terminated polyethylene oxide (PEO-NH₂), amino-terminated polyethylene glycol (PEG-NH₂), polypropylene glycol (PPG), polypropylene oxide (PPO), polypropylene glycol bis(2-amino-propyl ether) (PPG-NH₂), polyvinyl alcohol, poly(acrylic acid), poly(vinyl pyridine), poly(N-isopropylacrylamide) (polyNIPAM) and polyallylamine (PAM).

92. (Previously added) The method according to claim 91, wherein the water soluble polymer is selected from the group consisting of PEO, PEO-NH₂, PEG, PPG-NH₂, polyNIPAM and PAM.

93. (Previously added) The method according to claim 92, wherein the polymer is PEO.

94. (Previously added) The method according to claim 84, wherein the linker is selected from the group consisting of C₁₋₂₀alkylene, C₁₋₂₀alkenylene, organic ethers, thioethers, amines, esters, amides, urethanes, carbonates and ureas.

95. (Previously added) The method according to claim 84, wherein the compound of Formula I is selected from one or more of:

GluconamideSi (Compound 1);

MaltonamideSi (Compound 2);

DextronamideSi (Compound 3);

$(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)]_2$, $p \sim 4-5$, average MW 200 (Compound **5a**);
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)]_2$, $p \sim 13$, average MW 600 (Compound **5b**);
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)]_2$, $p \sim 44$, average MW 2000 (Compound **5c**); and
 $(\text{CH}_2\text{CH}_2\text{O})_p[(\text{EtO})_3\text{Si}(\text{C}_3\text{H}_6)]_2$, $p \sim 227$, average MW 10,000 (Compound **5d**).

96. (Previously added) The method according to claim 1, further comprising combining the organic polyol silane and one or more additives in the presence of one or more biomolecules.

97. (Previously added) The method according to claim 39, further comprising combining the organic polyol silane and one or more additives in the presence of one or more biomolecules.

98. (Previously added) The method according to claim 41, further comprising combining the organic polyol silane and one or more additives in the presence of one or more biomolecules.

~~40099~~. (Currently amended) A method for the quantitative or qualitative detection of a test substance that reacts with, binds to and/or whose reactivity is catalyzed by an active biological substance, wherein said biological substance is encapsulated within a siliceous material, comprising:

- (a) preparing the siliceous material comprising said active biological substance entrapped within a porous, silica matrix using a method according to claim 98;
- (b) bringing said biological-substance-containing siliceous material into contact with a gas or aqueous solution comprising the test substance; and
- (c) quantitatively or qualitatively detecting, observing or measuring the change in one or more characteristics in the biological substance entrapped within the siliceous material and/or, alternatively, quantitatively or qualitatively detecting, observing or measuring the change in one or more characteristics in the test substance.

404100. (Currently amended) The method according to claim 100, wherein the change in one or more characteristics of the entrapped biological substance is qualitatively or quantitatively measured by spectroscopy, utilizing one or more techniques selected from UV, IR, visible light, fluorescence, luminescence, absorption, emission, excitation and reflection.

402101. (Currently amended) A method of storing a biologically active biological substance in a silica matrix, wherein the biological substance is an active protein or active protein fragment, wherein the silica matrix prepared using a method according to claim 98.